<b>4</b> D	α τι	01.63				
54 A GCC	108 TAC Y	162 TCC S	216 ACC T	270 CCC P	324 CTC L	378 AGA R
GCA	ATC I	AAC N	ACG	ATG M	CAA Q	GAG ,
AGT	GCC	TGC	AAC N	ACC T	AAG ( K	GCT C
45 CCG	99 AAG K	153 TAC Y	207 CGG	261 CCC 7	315 ATC A I	369 TCT G S A
AGT	CCC	AAG K	CCT O		3 GCC A A I	3 CAG T Q S
AAA	CGG R	AGC S	CTG (	ATC G	GTG G V A	7 2 2 2 2 5 5 5 5
36 GTA	90 TAC ( Y	144 TTC ? F	198 GGC C G L			
<b>₽</b>				252 TCC S	306 CCT P	360 CGT R
ACA	AGC	ATC	ACC	GTC V	AGA R	AGC S
AGT	TCC	GTA V	GCC	ATG M	GTG V	ACA
27 GAA	81 TCC S	135 AAG K	189 ATC I	243 GCC A	297 AAA K	351 ACC / T
990	9 9	CAG Q	TGC	GAC D	TAC Y	AGA A
CGT	TCC	ATT I	TTC	GAC (	CCG 7 P 1	AAG A K R
18 TGG	72 GGA G	126 CGC R	180 CTG ' L	234 ACC ( T	288 ACT ( T	342 GAC A D K
	ATG M	GGA G	GAC (	ACC A	2 CGC A R T	3 GAG G E D
<u> </u>	AGG	7 C GAT ( D (	ATG G M L	Q A II	<b>₹</b> ₽₩	
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Ö	252 CGC	11. AT( I	171 ATC I	225 CTG L	279 TCA S	333 GGT G
CCC	999 JJ5	GAC	GAC D	ICC	AAT N	GCT A
9 5' GCT CCC CGC GGC GGC	၁၁၅	$^{ m CTG}$	AGC GAC ATC S D I	ATC	GCG 7	TCC C
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#### FIGURE 1A

432 GCA A	486 CAG Q		594 GAA E	648 AAA K	702 CTG	756 14C 1
. GGA	TAC Y	CTC	GCT A	CTA L	3AG E	GAT A
GAA E	TGC	GTG V	AAA K	3GA	3AG	
423 AGG R	477 GGC G	531 AGC S	585 CTG L	639 Gaa E	693 AGG R	747 [TT
CGG R	CAG Q	CAG 2	3AA 3	L.T.G	TG	AGT S
CCC	CCC	ATC I	AAT V	AAA	AG	AC
414 CAG Q	468 GAG E	522 TTA L	576 ATC I	630 3TG 7	584 \AG	738 4AG 5
GAG	AGA R	GAA E	AAA K	CGC R	ATT	lGT
CTG	CCC	GAA E	TTC F	AAA K	3AC	22
405 GGC G	459 AGG R	513 AGA R	567 GCA A	621 GAG /	675 AGT S	729 IGC (
	CCC	GAG E	AGA R	CTA L	AAG K	AAC N
GTT	GAG	CCA P	TCA S			ACC I
396 CGG R	450 GTA V	504 CCT P	558 TTC F	612 GCT A		720 AGG ,
AGA R	CAG Q	ATC I	CAG Q	TTG L	GAG E	AGC .
GAC D	GGA G	CGC R	GAG E	CAC H	\T\T	25
387 AGG R	441 A AGT S	495 CAG Q	0 K	<b>ε</b> Η	~ rn	1
CCA CTG P L	TTT GAA F E	0.00 0.00	GTT	GCA A	GTG V	GCC.
CCA	TTT	GAA E	CAG Q	GTT GCA AAY V A N	GTG V	GCG A

### FIGURE1B

#### CAC AAG AAG TTG ACT CCT CGA CGC GAT GTT CCC ACT TAC CCC AAG TAC CTG CTC H K K L T P R R D V P T Y P K Y L L GAG CCC AAT GAG ATG CTG AGC TGC CTG GAG CAC ATG TAC CAC GAC CTC GGG CTG EPNEMISCOT CTG CTG GAG CAC ATG TAC CAC GAC CTC GGG CTG 927 GTC AGG GAC TTC AGC ATC AAC CCT GTC ACC CTC AGG AGG TGG CTG TTC TGT GTC V R D F S I N P V T L R R W L F C V CAC GAC AAC TAC AGA AAC AAC CCC TTC CAC AAC TTC CGG CAC TGC TTC TGC GTG H D N Y R N N P F H N F R H C F C V 1035 1044 1053 1062 1071 1080 GCC CAG ATG TAC AGC ATG GTC TGG CTC TGC AGT CTC CAG GAG AAG TTC TCA A Q M M Y S M V W L C S L Q E K F S 1089 1098 1107 1116 1125 1134 CAA ACG GAT ATC CTA ATG ACA GCG GCC ATC TGC CAC GAT CTG GAC CAT Q T D I L I L M T A A I C H D L D H 1089

FIGURE 1C

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1 1170 1179 1188	5 1224 1233 1242	) 1278 1287 1296	1332 1341 1350	1395 1404	1440 1449 1458	1467 1476 1485 1494 1503 1512
C AAT GCC CGC ACA GAG CTG GCG GTC CGC	C CAC CAC TGC GCC GTG GCC TTC CAG ATC	TCC AAC ATC CCA CCT GAT GGG TTC AAG	. ATC TTG GCC ACT GAC ATG GCA AGA CAT	AAA ATG GAG AAT TTT GAC TAC AGC AAC	ATT TTG ATA AAA TGC TGT GAT ATC TCT	AAC GAG GTC CGT CCA ATG GAA GTC GCA GAG CCT TGG GTG GAC TGT TTA TTA GAG
N A R T E L A V R	H H C A V A F Q I	S N I P P D G F K	I L A T D M A R H	K M E N F D Y S N	I L I K C C D I S	N E V R P M E V A E P W V D C L L E
116	121	126:	132:	1377	1431	1485
C CAG AT	G GAG AA	3 ATC TT(	C ACA TTP	AAA GAG	AAG ATG	GTC GCA
Q I	E N	I F	T L	K E	K M	V A
1152	1206	1260	l314	.368	422	476
ACG TA	CCG CTA	TGC AA(	ATG ATC	TCT TTC	CTG CTG	ATG GAA
T Y	P L	C N	M I	S F	L L	M E
AAC AAC N N	ATC TCA I S	CCT GAG	cag gga 2 g	1 NTG GAT I D	1 TG ACC	T. GT CCA i
1143 CCC GGC TAC P G Y	1197 TAC AAT GAC Y N D	1251 CTC GCC GAG ( L A E 1	1305 CAG ATC CGA (	1359 SCA GAA ATT A	1413 AG GAG CAC A E H M	1467 AC GAG GTC C
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1566 3 GCA CCG A P	1620 C ATC AAG I K	1674 GTT GAG V E	1728 CTG AAG L K	1737 1746 1755 1764 1773 1782 GAT GAC GCC ATG AAA GAG TTA CAG AAG AAG ACT GAC AGC TTG ACG TCT D D A M K E L Q K K T D S L T S	1836 GAA GGA E G	1890 TGG CCG
, GTC V	TTC	ATG M	GAG E	$ ext{TTG}$	AGT	295
1557 ' CCT	1611 GGG G	1665 CCC P	1719 GAG E	773 AGC S	827 AAC N	381 ACG (
CTT	ATT I	TTC	1 TAC Y	1 GAC D	1 AAA , K	18 NGG 1
0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.0	CAG Q	CTC	CGC R	ACT	3TG 7	
1548 . GAA E	1602 GCC A	1656 AAG K	.710 GAT D	764 AAG K	818 3AT (	372 :AG 1
TCA	ACA T	ACC	1 CGA R	1 AAG K	AGA (	18 TG (
AAG K	GCC	GTG V	TCC	CAG	AGC 7	Jeg (
1539 ' GAG E	1593 AAG K	1647 ACA T	.701 GAA E	755 TTA L	809 AGA R	363 3CG 1
CGT	ACC	GAA E	1 TGG W	1 GAG E	1 3AG , E ]	18 3GG (
GAC	GTG V	T'T'T F	CTT L	AAA K	AGA (	) 993
1530 AGC S	1584 AAA K	1638 ATG M	.692 CCA P	746 ATG M	800 rcc 7	354 AAG (
CAG Q	GAC	CCA P	1 CAG Q	GCC A	AAG 7	18 3GA A
ATG M	CGA R	ATC I	CTG L	GAC D	3AG Z	GA C
1521 TTT F	1575 GAC D	1629 CTG L	.683 ATG M	737 GAT D	791 ACC ( F 1	345 3CC 1
1521 GAA TAT TTT E Y F	ATG	GTC V	1 ATC I	ATA I	1791 GCC ACC A T	18 FGT (
GAA E	TTC	1629 TTT GTC CTG F V L	1683 GAG ATC ATG E I M	CGG R	999	1845 GAC TGT GCC D C A

FIGURE 1E

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### FIGURE 1F

AGA CCA TGT TTT CTA AGA ACC ATT TTG TTC ACT GAT ACA AAA AAA AAA AA 3' 1899 1908 1917 1926 1935 1944 AGC TGC GCG GGA TCC TTG TGC AGG GAA GAG CTG CCC TGG GCA CCT GGC ACC ACA 

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### FIGURE 2A

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### FIGURE 2B

PDE9A PDE8A SI E A N Y H S L E D H Y V K DLGLVRDFSINPVTLRRWLFCVHDNYRFGICEFLHCSESTLRSWLQIIEANYSRELLTSLMIPPKTFLNFMSTLEDHY PLIYLGLKMFARF PLIYLGLKMFARF PLTCVAYTIFOSR Ø 272 397 204

PDE9A PDE8A STHSADVLHATAYFLSKERIKETLDPIDEVAALIA SLHAADVTOSTNVLLNTPALEGVETPLEVGGALFA QTDILILM LOEKFS ß LC SMVW FCVAOMMY ت ا Ы N P F H N N P Y H N NH Ľ Д Z 309 437

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g829179 PDE8A PDE9A ICHDLDHPGYNNTYQINARTELAVRYNDISPLENHHCAV TIHDVDHPGRTNSFLCNAGSELAILYNDTAVLESHHAAL CIHDVDHPGLTNQFLVNSSSELALMYNDESVLENHHLAV Ą Ø 349 477 284

PDE9A PDE8A EPE-CNIFSNIPPDGFKOIRQGMITLILATDMARGDDKCNIFKNMERNDYRTLROGIIDMVLATEMTKNQG-CDIFCNMQKKQRQTLRKMVIDIVLSTDMSK E O K AFOIL! AFOLT' AFKLL 517

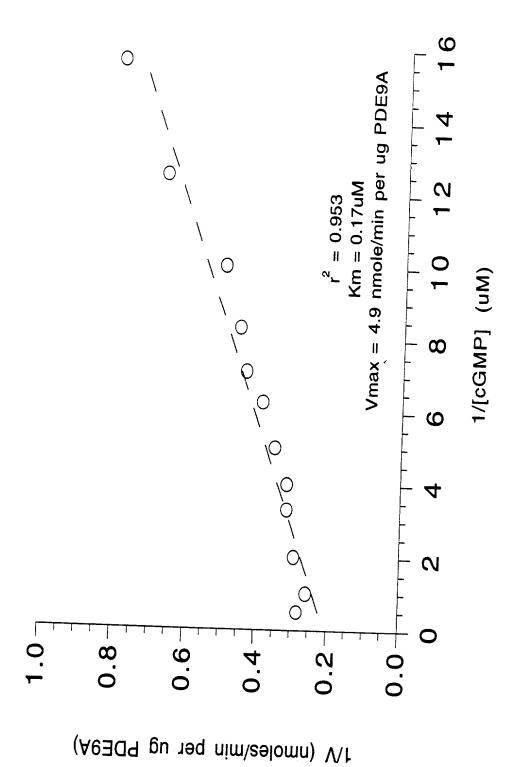
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### FIGURE 2D



FIGURE

cGMP Hydrolysis (% conversion)

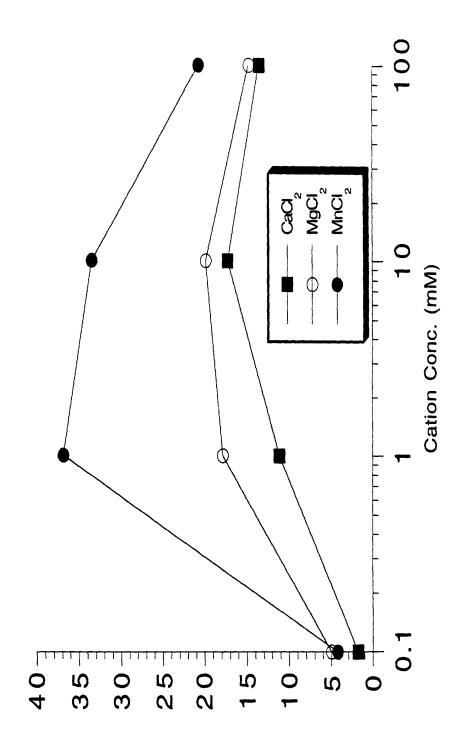


FIGURE 4

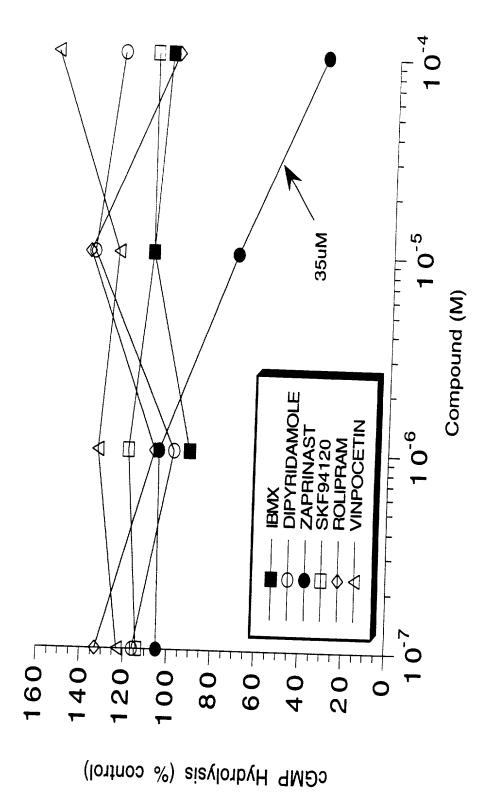


FIGURE 5